Studies of Negative Ions by Collision-Induced Decomposition and Hydrogen-Deuterium Exchange Techniques

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Development of two new techniques for studying the gas phase chemistry of negative ions is reported. Collision induced dissociation (CID) of (M-1)⁻ ions has been accomplished in a newly constructed triple stage quadrupole mass spectrometer. This instrument was assembled by adding two additional Finnigan quadrupole mass filters to a Finnigan Model 3200 CI mass spectrometer. Generation of (M-1)⁻ ions is accomplished by allowing OH⁻ and sample to react under CI conditions in the ion source. The first quadrupole mass filter, Q_1, is then employed to selectively pass the (M-1)⁻ ion into a second quadrupole filter containing argon or neon at 10^{-3} torr. On collision with the inert gas the (M-1)⁻ ions dissociate into fragments which are then mass analyzed in the third quadrupole filter. CID spectra of (M-1)⁻ ions from twelve carbonyl compounds are presented in this paper. Ion molecule isotope exchange reactions in the CI ion source can be used to count the number of hydrogen atoms in many different chemical environments. Collisions between sample (M-1)⁻ ions and deuterium-labeled reagent gases (ND_3, D_2O, EtOD) facilitate incorporation of deuterium into the negative ion if the basicities of the sample and reagent anions are similar. Thus it is possible to selectively incorporate deuterium into many organic samples by controlling the exothermicity of the acid base, ion-molecule chemistry.

Introduction

We report the development of two new techniques for studying the gas-phase chemistry of negative ions. In the first part of the paper we discuss the utility of a newly constructed triple-stage quadrupole (TSQ) mass spectrometer for obtaining collision-induced dissociation (CID) mass spectra of $(M - 1)^-$ ions. Examples of gas phase ion/molecule isotope exchange reactions are presented in the second part of the paper.

Collision-Induced Dissociation of Negative Ions in a Triple-Stage Quadrupole Mass Spectrometer

It has recently been shown that multistage mass spectrometers consisting of an ion source, mass analyzer, collision gas chamber, and second analyzer can be used in place of combined gas chromatography mass spectrometry for the analysis of complex mixtures of organic compounds. (1) In the latter technique, neutral mixture components are separated chromatographically, and each molecule is then ionized separately and characterized by its molecular weight and fragmentation pattern. In the multistage mass spectrome-

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try methodology, ions characteristic of molecular weight are generated from all mixture components simultaneously. Each ionized mixture component is then separated in a mass analyzer, caused to fragment in a gas collision chamber, and identified from the mass spectrum of the resulting fragment ions. To investigate the collision induced dissociation of negative ions we have constructed a triple stage quadrupole instrument similar in design to that described by Enke and Yost (2). The first and third quadrupoles in this instrument function as conventional mass filters. The middle quadrupole operates with rf voltage only on the rods and serves both as a collision cell and an ion trap. The sensitivity of this new instrument is comparable to that obtained on conventional single quadrupole GC-MS equipment.

Construction and Operation of TSQMS for CID Studies

Construction of this unit was accomplished by adding two additional Finnigan quadrupole mass filters to a Finnigan Model 3200 quadrupole CI mass spectrometer. The resulting system (Fig. 1) consists of a Model 3200 CI ion source, source lens, two Model 3200 mass filters (Q_1 and Q_2), a Model 4000 quadrupole mass filter (Q_3), and a conversion dynode electron multiplier detector for recording either positive and negative ions. Lenses 1-6 have aperture diameters of 3 mm. Operation of this system does not require vacuum pumping capacity beyond that normally provided with a single stage Finnigan Model 3200 CI system.

To utilize the TSQMS for CID studies of negative ions the ion source potential is set between −10 and −15 V, and all lens voltages are optimized at positive values. Q_1 is the set to pass the ion of interest into Q_2. Only rf voltage is placed on the rods in Q_2. In this mode, Q_2 functions as an ion trap and transmits ions of all masses. Collision gas pressures between 1 and 6 × 10^{-3} torr in Q_2 are required to optimize formation and collection of fragment ions. A draw-out potential of +10 to +30 V is placed on Q_3 which in turn functions as a normal quadrupole mass filter and mass analyzes the fragment ions produced in Q_2. Both argon and neon were used as collision gases.

Results and Discussion

Table 1 contains the CID mass spectra of (M - 1)⁻ ions generated from 12 compounds containing a carbonyl group. Production of (M - 1)⁻ ions was accomplished by using OH⁻ as the CI r~ actant. This in turn was generated by the method
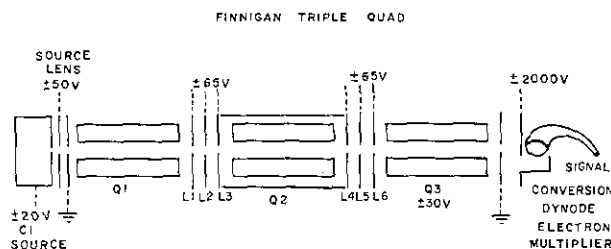

FIGURE 1. TSQMS unit.

of Field and Smith using a mixture of CH_4/N_2O as reagent gas under NICI conditions (3). Reaction of OH⁻ with compounds 1-10 (Table 1) affords only (M − 1)⁻ ions. One explanation of this result assumes that the lifetime of the ion/molecule complex is short and, therefore, the exothermicity of the reaction remains largely in the new bond that forms. As shown in Eq. (1), the new bond is in the reagent gas molecule and not in the sample ion. Accordingly the (M − 1)⁻ ions are produced with little excess energy and, therefore, suffer little or no fragmentation.

$$OH^{(-)} + CH_3COCH_3 \rightarrow H_2O + CH_3COCH_2^{(-)} \tag{1}$$
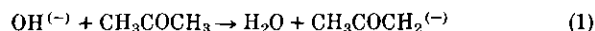
After passage through the first mass filter, Q_1, the (M − 1)⁻ ion enters Q_2 where it becomes vibrationally excited during collisions with either argon or neon atoms. Carbanions can acquire 2 or 3 eV of internal energy by this mechanism in the TSQ instrument. Accordingly dissociation pathways which are either endothermic or which involve considerable activation energy now become accessible and considerable fragmentation of the ion occurs.

A major fragmentation pathway observed for all ketones and aldehydes studied involves loss of H_2 from the (M − 1)⁻ ion. Formation of a conjugated anion presumably provides the driving force for this reaction. Carbanions derived from ketones also suffer loss of alkene molecules. This reaction is dependent on the position of the carbonyl group in the molecule and probably involves hydrogen transfer via a six-membered transition state as shown in Eqs. (2) and (3)
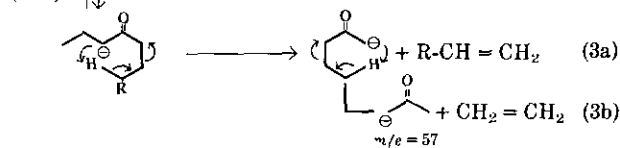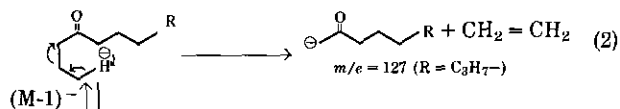
For R = C_3H_7; $\Delta H_2 = 22.5$, $\Delta H_{3a} = 20$, $\Delta H_{3b} = 22.5$
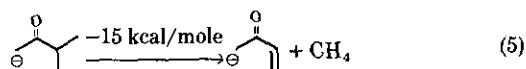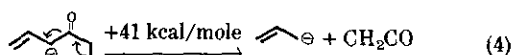
Table 1. CID mass spectra of $(M-1)^-$ ions generated under negative ion CI conditions with CH_4/N_2O as the reagent.[a]

| Compound	No.	MW	E_{CID}, %[b]	Total negative sample ion current, %						
				$(M-1)^-$	$(M-3)^-$	$RCO\text{-}CH_2^-$	(m/e)	R	$(M-ROH)^-$	Other: %, (m/e)
3-Decanone	I	156	11	66.0	6.1	13.1	(71)	Et	—	4.3(127), 4.3(125), 6.2(83)
4-Decanone	II	156	14	63.0	4.0	10.5	(127)	$n\text{-}C_6H_{11}$	—	5.5(139), 2.0(111), 2.5(97)
						9.5	(85)	$n\text{-}C_3H_7$		
						3.0	(57)	H		
3-Penten-2-one	III	84	20	67.0	2.8	—	—	—	—	1.4(69), 1.4(65), 1.4(55), 26.0(41)
3-Methyl-2-butanone	IV	86	3	75.0	2.5	—	—	—	—	1.5(69), 2.5(57), 2.5(43), 2.5(41)
Cyclohexanone	V	98	16	56.1	37.3	5.0	(69)	C_2H_4	—	1.6(41)
2-Methylcyclohexanone	VI	112	10	55.0	25.7	6.7	(83)	C_3H_6	—	1.7(95), 1.7(93), 1.7(69), 1.7(67), 1.8(57), 2.7(55), 2.7(41)
Nonyl aldehyde	VII	142	8	19.5	17.5	—	—	—	—	2.8(137), 2.8(113), 1.8(99), 1.6(83), 1.5(71), 10.8(55), 1.7(43)
Ethyl hexanoate	VIII	144	20	42.0	—	—	—	—	49.2	1.7(115), 1.5(113), 1.5(111), 1.5(77), 2.6(45)
Methyl crotonate	IX	100	25	37.5	—	—	—	—	57.5	5.0(55)
n-Pentyl acetate	X	130	30	40.0	—	—	—	—	60.0	—
Dimethyl suberate	XI	202	45	11.5	—	—	—	—	60.5	11.5(137), 1.0(111), 1.0(109), 11.5(93), 1.0(81), 1.0(73), 1.0(41)
Glucose	XII	180	80	7.5	—	—	—	—	—	2.0(161), 2.0(149), 2.0(143), 2.0(131), 10.0(119), 7.0(113), 2.0(107), 5.0(101), 46.5(89), 7.0(71), 7.0(59)

[a] Ion source temperature, 100°C; ion source pressure, 0.5 torr; collision gas, Ar for 3- and 4-decanone, Ne for all other compounds.
[b] Efficiency of the CID process as measured by dividing the sum of the ion currents due to fragment ions produced on collision, by the ion current carried by the $(M-1)^-$ ion in the absence of collision gas. This number is then multiplied by 100.

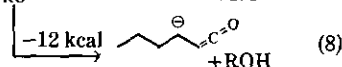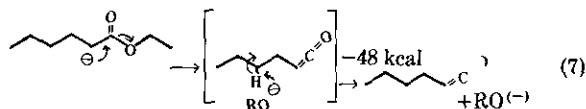kcal/mole. The values of ΔH were obtained by using literature data and the Group Equivalent Method.

This mechanism predicts that compounds I and II in Table 1 should afford one and three fragments ions respectively from the olefin elimination pathway. This is the observed result. Compounds III and IV lack the structural requirements for the above rearrangement and thus fail to eliminate alkene. Dissociation of $(M-1)^-$ ions from these compounds occurs by an alternative pathway involving loss of ketene and methane respectively as shown in Eqs. (4) and (5).

$$\text{(structure)} \xrightarrow{+41\text{ kcal/mole}} \text{(structure)} \ominus + CH_2CO \qquad (4)$$

$$\text{(structure)} \xrightarrow{-15\text{ kcal/mole}} \text{(structure)} + CH_4 \qquad (5)$$

Elimination of olefin is also a major pathway in the CID of $(M-1)^-$ ions from cyclohexanones. Compounds V and VI eliminate C_2H_4 by what appears to be an anionic retro Diels-Alder reaction [Eq. (6)].

$$\text{(structure)} \xrightarrow{+35\text{ kcal/mole}} \text{(structure)} \ominus \leftrightarrow \text{(structure)} \qquad (6)$$
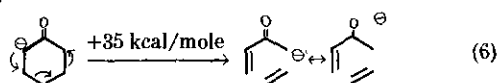
CID of $(M-1)^-$ ions from esters presumably occurs by a two step process involving dissociaton into RO^- and ketene molecule, which then undergo a proton transfer reaction during the lifetime of the ion/molecule complex to produce neutral alcohol and a ketene anion [Eqs. (7) and (8)]

$$\text{(structure)} \rightarrow \left[\text{(structure)} \right] \begin{array}{l} \xrightarrow{-48\text{ kcal}} \text{(structure)} \\ +RO^{(-)} \end{array} \qquad (7)$$

$$\xrightarrow{-12\text{ kcal}} \begin{array}{l} \text{(structure)} \\ +ROH \end{array} \qquad (8)$$

The TSQ low energy CID spectrum of the $(M-1)^-$ ion from glucose is identical to that obtained in the high energy MIKES experiment by Cooks et al. (1). The spectrum can be adequately explained by a combination of carbonyl group isomerization, anionic retro aldol condensation, and dehydration reactions, as shown in Eq. (9).
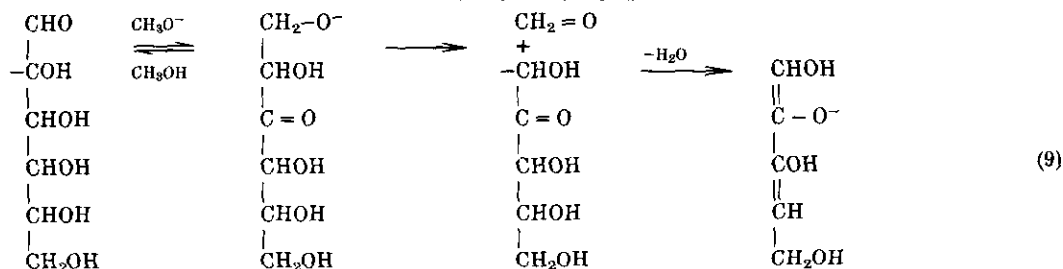
Results presented here suggest that CID spectra of $(M-1)^-$ ions will afford excellent structural information from many molecules. Since $(M-1)^-$ ions can be generated under CI conditions without extensive fragmentation in the ion source, the above methodology should find considerable utility in the direct analyses of complex mixtures by multianalyzer mass spectrometers.

Hydrogen-Deuterium Ion/Molecule Isotope Exchange Reactions:

Negative ion/molecule hydrogen-deuterium exchange reactions in the gas phase were first reported by Shapiro et. al. (4). They showed that a host of $(M-1)^-$ ions suffered hydrogen-deuterium exchange on reactions with D_2O under "flowing afterglow" conditions. Reactions of D_2O with carbanions derived from ketenes and aldehydes, however, did not undergo isotope exchange. Two later studies showed that these $(M-1)^-$ ions do undergo exchange if CH_3OD is used as reagent gas instead of D_2O (5, 6). We have now studied negative ion/molecule isotope exchange reactions using four reagent gases, ND_3, D_2O, C_2H_5OD and CF_3CD_2OD under CIMS conditions (7). The reagent anions from each of these gases have different proton affinities and can be used to selectively abstract protons from different sites in sample molecules. The $(M-1)^-$ ions so produced react with neutral deuterated reagent gas molecules and undergo isotope exchange at only certain sites in the sample molecules. By using these reactions it is possible to use mass spectrometry to locate and count hydrogens in different chemical environments in a sample molecule.

A summary of negative ion/molecule isotope exchange reactions is presented in Table 2. Reagent ion ND_2^- is the most basic species (PA = 403 kcal/mole) we have generated under NICI conditions. With this reagent proton abstraction from benzene and polyaromatic hydrocarbons is exothermic, and the resulting $(M-1)^-$ ions undergo extensive incorporation of deuterium atoms on subsequent reactions with neutral ND_3 molecules.

CHO	CH_3O^-	CH_2-O^-		$CH_2 = O$		
|	$\rightleftharpoons$	|	$\longrightarrow$	+	$\xrightarrow{-H_2O}$	
$-COH$	CH_3OH	CHOH		$-CHOH$		CHOH
|		|		|		||
CHOH		$C=O$		$C=O$		$C-O^-$
|		|		|		|
CHOH		CHOH		CHOH		COH	(9)
|		|		|		||
CHOH		CHOH		CHOH		CH
|		|		|		|
CH_2OH		CH_2OH		CH_2OH		CH_2OH

Table 2. Summary of negative ion-molecule isotope exchange reactions.

Compound	No.	MW	Reagent gas[a]	$(M-1)^-$	d_1 $(M-1)^-$	d_2 $(M-1)^-$	d_3 $(M-1)^-$	d_4 $(M-1)^-$	d_5 $(M-1)^-$	d_6 $(M-1)^-$	d_7 $(M-1)^-$	Other m/e (%)
							Sample ion current, %[b]					
Benzene	XIII	78	ND_3	12.0	12.0	12.0	12.0	20.0	32.0	13.8	—	—
Naphthalene	XIV	128	ND_3	6.9	10.3	11.7	13.8	10.3	12.4	—	20.7	—
o-Xylene	XV	106	D_2O	8.5	8.5	14.0	14.0	14.0	55.0	—	—	—
2-Decanone	XVI	156	D_2O	65.5	21.8	8.7	3.9	—	—	—	—	—
2-Decanone	XVII	156	C_2H_5OD	2.8	2.8	5.6	16.7	72.2	—	—	—	—
2,2,4; 4,17,21,21-d_8-5α-Pregnan-3,17-dione[c]	XVIII	324	C_2H_5OH	13.3	16.4	18.8	17.2	12.5	10.2	7.0	4.7	—
Ethyl butyrate	XIX	116	C_2H_5OD	9.1	90.9	—	—	—	—	—	—	—
n-Butyraldehyde	XX	72	C_2H_5OD	26.0	74.0	—	—	—	—	—	—	—
Diethyl succinate	XXI	174	C_2H_5OD	8.7	9.8	16.3	65.2	—	—	—	—	87 (3.1), 88 (12.4), 89 (52.8), 159 (11.2)
Diethyl glutarate	XXII	188	C_2H_5OD	6.2	6.2	4.4	3.7	—	—	—	—	
Diethyl malonate	XXIII	160	C_2H_5OD	88.9	11.1	—	—	—	—	—	—	—
Diethyl malonate	XXIV	160	CF_3CD_2OD	55.0	45.0	—	—	—	—	—	—	—

[a] All spectra were recorded on AEI MS-902 mass spectrometer, at ion source temperature of 175°C.

[b] The spectra are not corrected for C^{13} contributions.

[c] The $d_n(M-1)^-$ ions in this spectrum represent sequential loss of deuterium from the $(M-D)^-$ ion.

In contrast to the above situation, ND_2^- abstracts proton from benzylic positions but the resulting anions fail to incorporate deuterium on collision with ND_3. We suggest that this is because the reverse reaction is too endothermic. The exchange of benzylic hydrogens can, however, be accomplished by using OD^- in D_2O as the reagent ion. The base strength of OD^- is such that it can abstract benzylic protons but not aromatic protons. Accordingly selective exchange of benzylic protons is observed with this reagent.

Ketones, esters, diesters, and aldehydes produce $(M - 1)^-$ ions on reaction with OD^+, but fail to undergo isotope exchange. Incorporation of deuterium into these anions is observed, however, if weaker bases are employed in the ionization step. Use of C_2H_5OD/N_2O mixtures affords $C_2H_5O^-$ reagent ions. This reagent fails to abstract benzylic hydrogens but does react with ketones, esters, diesters, and aldehydes. The resulting $(M - 1)^-$ ions readily undergo isotope exchange reactions with C_2H_5OD and incorporate deuterium at all positions alpha to the carbonyl group in the molecule. To confirm the site specificity of the exchange process the deuterium labeled steroid XVIII was examined with unlabeled reagent gas, C_2H_5OH. All the deuterium atoms in compound XVIII suffered at least partial exchange in this experiment.

The $(M - 1)^-$ ions of ethyl butyrate and butyraldehyde exchange only the alpha hydrogen with deuterium when $C_2H_5O^-/C_2H_5OD$ is employed as reagent. Proton abstraction from diethyl succinate and glutarate can occur from methylene groups alpha to both the carbonyl groups. All these hydrogens suffer exchange. The $(M-1)^-$ ion of XXII also undergoes fragmentation by a retro Michael addition reaction to produce the ion at m/e 89 [Eq. (10)],

$$d_3(M\text{-}1)^- \; m/e = 190 \qquad m/e = 89$$
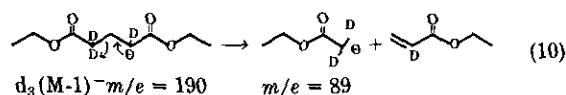
Hydrogen atoms on a methylene group adjacent to two carbonyl groups, as in diethyl malonate are too acidic to suffer exchange with C_2H_5OD, but do undergo the gas phase ion/molecule isotope exchange reaction when the weaker base $CF_3CD_2O^-$ is employed as reagent.

Ion/molecule reactions reported here can be utilized to locate and count hydrogen atoms in different chemical environments. The information obtained is similar to that available from NMR chemical shift and integration measurements. Only nanogram samples are required for the mass spectrometry experiments.

REFERENCES

1. McClusky, G. A., Kondrat, R. W., and Cooks, R. G., Direct mixture analysis by mass-analyzed ion kinetic energy spectrometry using negative chemical ionization. J. Am. Chem. Soc. 100: 6045 (1978).
2. Enke, C., and Yost, R., Selected ion fragmentation with a tandem quadrupole mass spectrometer. J. Am. Chem. Soc., 100: 2274 (1978).
3. Smit, A. L. C., and Field, F. H., Gaseous anion chemistry. Formation and reactions of OH^-; reactions of N_2O; OH^- negative chemical ionization. J. Am. Chem. Soc., 99: 6471 (1977).
4. Stewart, J. H., et al., Hydrogen-deuterium exchange reactions of carbanion with D_2O in the gas phase. J. Am. Chem. Soc., 99: 7650 (1977).
5. Hunt, D. F., Plenary lecture presented at the Ninth British Mass Spectroscopy Group meeting at the University of Swansea, England, September 27-29, 1977.
6. DePuy, C. H. et al., Hydrogen-deuterium exchange reactions of carbanions with deuterated alcohols in the gas phase. J. Am. Chem. Soc., 100: 2921 (1978).
7. Hunt, D. F., Sethi, S. K., and Shabanowitz, J., Ion-molecule isotope exchange reactions: methodology for locating protons in sample molecules. Paper presented at the 26th Annual Conference on Mass Spectrometry and Allied Topics, St. Louis, May 28-June 3, 1978, paper no. MF-1.